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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,193	08/26/2003	Marilyn H. Perrin	SALK1740-10 (088802-3218)	5260

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EXAMINER	
BORGEEST, CHRISTINA M	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 11/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/649,193	PERRIN ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6 September 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Formal Matters

The amendment filed 6 September 2006 is acknowledged. Claims 1, 3, 4, 5, 6, 7, 11, 13 15, 17 are amended. Claim 20 is new. Claim 12 is cancelled. It is noted that Applicants' correspondence in their reply to the first office action makes reference to a new claim 21 (see p. 6, 3rd paragraph), however, this claim cannot be found among any of the materials filed by Applicants, thus only claims 1-11 and 13-20 can be considered under examination at this time.

The text of those sections of 35 U.S.C. not included in this action can be found in a prior office action mailed 1 May 2006.

Rejections/Objections Withdrawn

The objection to claims 1-11 and 13-19 because the claims recite non-elected species SEQ ID NOs: 5, 6, 7, 8, 9 10 as set forth at p. 3 of the previous office action (mailed 1 May 2006) is withdrawn in response to Applicants amendment of the claims in the response filed 6 September 2006.

Priority

Applicant's claim for receiving the benefit of an earlier filing date under 35 U.S.C. [120] of 23 August 1993 was acknowledged but not granted by the Examiner, and the

effective filing date determined by the Examiner was 12 November 1998, as set forth at p. 3 of the previous Office action (mailed 1 May 2006).

Applicants disagree with the Examiner's assertion that the earlier filed applications, namely Application Nos. 08/483,139, 08/343,537 and 08/079,320 do not provide support for SEQ ID NOs: 14 or 15. Applicants assert that they are entitled to a priority date of 23 August 1993, the filing date of Application NO. 08/110,286, now U.S. Patent No. 5,728,545 (the '545 patent). Applicants assert at p. 7, 3rd and 4th paragraphs that: claims 13 and 14 are directed to SEQ ID NO: 15, an exemplary sequence of hCRF-RA_2, which is a splice variant of hCRF-RA_1 that includes a 29 amino acid insert located between amino acid residues 145 and 146 of hCRF-RA_1 and that SEQ ID NO: 15 is fully supported by the disclosure of the '545 patent because sequence of SEQ ID NO: 2 (amino acid sequence of hCRF-RA_1), presented at col. 31-34, is identical to SEQ ID NO: 2 of the present application; sequence of SEQ ID NO:4 (the 29 amino acid insert), presented at col. 35, is identical to SEQ ID NO:4 of the present application; and the location of the 29 amino acid insert is specified at col. 28, lines 55-59; i.e., between residues 145 and 146 of hCRF-RA_1, consistent with the location specified in the present application. Thus, SEQ ID NO: 15 simply shows the sequence resulting from the incorporation of SEQ ID NO: 4 between residues 145 and 146 of SEQ ID NO: 2. Likewise, Applicants make a similar argument with regard to the nucleotide (SEQ ID NO: 14—see p. 8, 2nd – 4th paragraphs).

These arguments have been fully considered but are not persuasive. According to MPEP 201.11, the last filed application (that has the claimed subject matter in

question) must have at least two things to get benefit to the earliest application which discloses that claimed subject matter: continuity via copendency in the chain of intervening applications and continuity of subject matter in the chain of intervening applications. If applicant deletes/removes the claimed/disclosed subject matter from any of the intervening copending applications, AND the earliest application having that subject matter became abandoned or allowed BEFORE the filing of the last application, then applicant cannot skip over the intervening applications to obtain benefit of that subject matter. The '545 patent was allowed BEFORE the filing (issued 17 March 1998) of the last application, thus Applicant effectively abandoned that subject matter for benefit of priority claim in the instant application, which can claim benefit of Application No. 09/191,724, filed 12 November 1998, and the determination of the effective filing date as ***12 November 1998*** is maintained.

Information Disclosure Statement

The objection to the information disclosure statement (IDS) filed 12 November 2003 for failing to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 as set forth at p. 4 because it includes 2 pages from a previous 892 form cited in a previous case and the references are not in proper form to be considered is withdrawn in response to Applicants submission of a new IDS 6 September 2006.

Claim Rejections - 35 USC § 102

The rejection of claim 12 under 35 U.S.C. 102(b) as being anticipated by Laurent et al. (FEBS, 1993; 335: 1-5), as set forth at pages 8-9 is withdrawn in response to Applicants' cancellation of claim 12 in the response filed 6 September 2006.

Rejections Maintained

Claim Rejections - 35 USC § 112, second paragraph

The rejection of claim 1, and claims 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, which depend from 1, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention as set forth at pages 4-5 is maintained for reasons of record and the following.

To summarize the previous rejection: Claim 1 recites "suitable stringency" which is indefinite, because it does not define clearly the hybridization and wash conditions required, thus leaves open the identity of the nucleic acid sequences that would hybridize to the complement of SEQ ID NO: 14. See MPEP 2173:

> The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent. A secondary purpose is to provide a clear measure of what applicants regard as the invention so that it can be determined whether the claimed invention meets all the criteria for patentability and whether the specification meets the criteria of 35 U.S.C. 112, first paragraph with respect to the claimed invention.

Neither the specification nor the art provides an unambiguous definition for "suitable stringency", therefore, the metes and bounds of the claimed invention cannot be determined.

Applicants amended claim 1 to replace "suitable stringency" with "low stringency," which they state is described in the specification.

Applicants argue at p. 9, last paragraph to p. 10, 3rd paragraph that one of skill in the art would understand how to adjust hybridization and wash conditions in order to achieve a particular level of identity and that there is guidance in the specification regarding the level of stringency of hybridization that one would use to achieve a particular level of nucleic acid identity, for example, "low stringency conditions" are described at page 43, line 20 to page 44,13 as conditions "which allow the identification of sequence which have a substantial degree of similarity (i.e., at least 50%homology) with the probe sequence," and are further described as comprising "a temperature of less than 42.5 °C, a formamide concentration of less than about 50%, and a moderate to low salt concentration."

This argument has been fully considered but is not found persuasive for the following reasons. The definitions in the specification and the literature of suitable, low, moderate, etc. stringency are open ended, thus the metes and bounds of the claims cannot be known, and the rejection is maintained.

Claim Rejections - 35 USC § 112, first paragraph

The rejection of claims 1-6, 8-11, 13-19 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the clamed inventions wherein the recited isolated protein comprises SEQ ID NO: 15 or an antigenic fragment thereof, does not enable the claimed invention broadly reciting variants and immunogenic fragments of SEQ ID NO: 15 at pages 5-8 is maintained for reasons of record and the

following. In addition, newly added claim 20 is also rejected under 35 U.S.C. 112, first paragraph.

To summarize the previous rejection: There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 Fed. Cir. 1988) These factors include, but are not limited to: (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claims are very broad; the variants as claimed read on a huge group of polypeptides. For instance, Claims 1-6, 8-10 and 15-19 claim the protein in terms of being encoded by polynucleotides that hybridize under suitable stringency to the complement of SEQ ID NO: 14. Although hybridization and wash conditions are recited, the use of the open language, "comprising", allows for the rehybridization and washing at lower stringency, thus many more polynucleotides than those that are complements of SEQ ID NO: 14 could potentially hybridize to SEQ ID NO: 14. Furthermore, the state of the art teaches that the temperature and salt concentrations at which hybridization is performed directly affects the results obtained. The conditions can be adjusted so the hybridzation is to a nucleic acid that has a lower degree of homology to the probe. See the website found at North Dakota State University, with regards to nucleic acid hybridization (ndsu.nodak.edu/instruct/mcclean/plsc731/dna/dna6.htm—accessed 7 April 2006). This also means that there is a degree of unpredictability as to what will hybridize to the complement of SEQ ID NO: 14, if the hybridization conditions are left open, as is the case in the claims.

In addition, the "immunogenic fragment" recited in claim 11 reads on any fragment of the protein, including a peptide consisting of 3-5 amino acids that is capable of inducing a general immune response. In the absence of any structural or functional limitations, the claim reads on any fragment of a G protein-coupled CRF receptor protein, and there are a huge number of polypeptides that would meet these criteria. The Applicants have provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, what polynucleotides would hybridize to SEQ ID NO: 14 and the immunogenic fragments that are encompassed in the claim. There is not adequate guidance as to the nature of immunogenic fragments.

The claims amount to single means claims. Single means claims are those that cover every conceivable means for achieving the stated purpose. Single means claims are nonenabling for the scope of the claim because the specification discloses at most only those means known to the inventor, in this case, a protein that is encoded by a polynucleotide consisting of SEQ ID NO: 14. When claims depend on a recited

property, i.e., the ability of a polynucleotide to hybridize under any conditions to the complement of a recited sequence, a fact situation comparable to Hyatt is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See MPEP 2164.08(a).

Due to the large quantity of experimentation necessary to generate the vast number of variants and immunogenic fragments of SEQ ID NO: 15 as recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of changing hybridization conditions (see discussion above and recited reference) and the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Applicants have amended the claims to recite "antigenic" fragments, thus the arguments at p. 11, last paragraph to p. 12, 1st paragraph, which relate to the definition of immunogenic will not be addressed.

Applicants disagree at p. 10, last paragraph and p. 11, 1st paragraph with the Examiner's assertion that the variants as claimed encompass a huge group of polypeptides because the contemplated variants must bind CRF and be encoded by DNA that hybridizes under moderately stringent conditions to the complement of the polynucleotide sequence set forth in SEQ NO: 14 and has at least 60% nucleic acid identity with respect to SEQ ID NO:14.

Applicants disagree at p. 11, 2nd paragraph with the Examiner's assertion that "[a]lthough hybridization and wash conditions are recited (in claim 15), the use of open language, "comprising", allows for the rehybridization and washing at lower stringency, thus many more polynucleotides than those that are complements of SEQ ID NO: 14 could potentially hybridize to SEQ ID NO: 14." Applicants argue that this concern is

unfounded because the term "comprising" is used with reference to hybridization and wash conditions, not steps in a hybridization procedure, therefore the Examiner's concern is not relevant, because in order to meet the requirements of the claim, a DNA must hybridize to the complement of SEQ ID NO: 14 under the recited hybridization and wash conditions and have the required property of binding CRF and that one of skill in the art would therefore readily appreciate that any polynucleotide identified under lower stringency conditions would not hybridize under the recited conditions, and therefore would not meet the requirements of the claim with respect to hybridization, minimum percent identity to the reference sequence, and binding CRF.

Applicants' arguments have been fully considered but are not found persuasive for the following reasons. First, with regard to Applicants' argument that the claims do not encompass a huge number of variants, the claims require a functional activity (binding to CRF) but with only limited structural conservation. The amount of experimentation required to test all the variants that could be encoded by DNA that hybridizes under moderately stringent conditions to the complement of the polynucleotide sequence set forth in SEQ NO: 14 and has at least 60% nucleic acid identity with respect to SEQ ID NO: 14 and screen the same for activity is undue, as was stated in the previous office action (mailed 1 May 2006). Applicants have merely stated they disagree with the Examiner's assertion, but absent facts or evidence to the contrary, the claims still encompass non-functional polypeptides that require further testing for activity. Second with regard to Applicants' argument that the Examiner's concern is unfounded because the term "comprising" is used with reference to

hybridization and wash conditions, not steps in a hybridization procedure, the Office is bound to give the broadest reasonable interpretation of the claims, and furthermore, wash conditions are important. The issue is that the hybridization conditions do not describe what will stick to the probe, particularly at low stringency. The definitions in the specification are open-ended, thus do not provide definitive conditions of stringency. As stated in the previous office action, the claims encompass a huge number of variants that would have to be tested for activity, thus the rejection of claims 1-6, 8-11, 13-19 for lack of enablement is maintained.

Claim Rejections - 35 USC § 102

The rejection of claims 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, 17, 18 and 19 under 35 U.S.C. 102(b) as being anticipated by Laurent et al. (FEBS, 1993; 335: 1-5) is maintained for reasons of record and the following. In addition, new cliam 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Laurent et al.

To summarize the previous rejection: Claims 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, 17, 18 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Laurent et al. (FEBS, 1993; 335: 1-5). Laurent et al. teach a membrane bound G protein coupled receptor that consists of the SEQ ID 15 and is encoded by the polynucleotide consisting of SEQ ID NO: 14. Because the exact sequence of SEQ ID NO: 15 (claims 7, 10—see entire document, for instance, p. 2, Figure 1) is disclosed in this reference, the limitations of claims 1, 11, 15-19 (the protein is encoded by DNA that hybridizes to the complement of SEQ ID NO: 14), 2 (having sufficient binding affinity for CRF such that concentrations of 10 nanomolar CRF occupy greater than or equal to 50% of binding sites...), 3-6 (encoded by DNA having at least 60/70/80/90% nucleic acid identity to the reference polynucleotide sequences), 9, 16, 18 (product by process claims; a product disclosed in the prior art, made by a different process, does not render the claims patentable) are met by Laurent et al., thus the claims do not contribute anything new over the prior art.

Applicants' argue at p. 12, 3rd paragraph that because they are entitled to a priority date of 23 August 1993, Laurent et al. is not available as prior art with respect to the present claims.

This argument has been fully considered but is not found persuasive because as discussed above under Priority, Applicants cannot skip over intervening applications to grab subject matter filed in a prior application that was allowed before the filing of the instant application, thus the effective filing date is 12 November 1998, and the reference by Laurent et al. is available as prior art with respect to the present claims.

The rejection of claims 1, 8 13 and 14 under 35 U.S.C. 102(b) as being anticipated by Chen et al. (Proc Natl Acad Sci. 1993; 90: 8967-8971—on IDS filed 12 November 2003) is maintained for reaons of record and the following.

To summarize the previous rejection: Claims 1, 8 13 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (Proc Natl Acad Sci. 1993; 90: 8967-8971—on IDS filed 12 November 2003). Chen et al. teach an isolated G protein-coupled corticotrophin releasing factor receptor that consists of the SEQ ID 15 and is encoded by the polynucleotide consisting of SEQ ID NO: 14. Because the exact sequence of SEQ ID NO: 15 is disclosed in this reference (see, for instance, Figure 2), the limitations of claims 1 and 13 (the protein is encoded by DNA that hybridizes to the complement of SEQ ID NO: 14) are met. In addition, Chen et al. teach a radioreceptor assay of the cloned receptor (see p 8967 under Materials and Methods, right column, 5th paragraph), and a polypeptide according to claim 13 in which a cysteine is attached by a peptide bond to the carboxyl terminus of said polypeptide (p. 8969, Figure 2), thus the claims do not contribute anything new over the prior art.

Applicants' argue at p. 13, 1st paragraph that because they are entitled to a priority date of 23 August 1993 is persuasive, Chen et al. is not available as prior art.

This argument has been fully considered but is not found persuasive because as discussed above under Priority, Applicants cannot skip over intervening applications to

grab subject matter filed in a prior application that was allowed before the filing of the instant application, thus the effective filing date is 12 November 1998, and the reference by Chen et al. is available as prior art with respect to the present claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11 and 13-20 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 5,728,545 (the '545 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '545 patent are drawn to a more specific embodiment of the polypeptides and polynucleotides recited in the instant claims. ***Applicants' explanation of priority revealed that the Patent Office***

should have made a rejection on the ground of nonstatutory obviousness-type double patenting over the '545 patent. As pointed out by Applicants at pages 7-8 of their response filed 6 September 2006, claims 13 and 14 of the instant application are directed to SEQ ID NO: 15, an exemplary sequence of hCRF-RA_2, hCRF which is a splice variant of hCRF-RA_1 that includes a 29 amino acid insert located between amino acid residues 145 and 146 of hCRF-RA1 SEQ ID NO: 15. SEQ ID NO: 2 of the '545 patent (amino acid sequence of hCRF-RA_1) is identical to SEQ ID NO: 2 of the instant application and SEQ ID NO: 4 of the '545 patent (the 29 amino acid insert) is identical to SEQ ID NO: 4 of the present application and the location of the 29 amino acid insert is specified between residues 145 and 146 of hCRF-RA_1, consistent with the location specified in the present application. Thus, SEQ ID NO: 15 of the instant application simply shows the sequence resulting from the incorporation of SEQ ID NO: 4 between residues 145 and 146 of SEQ ID NO: 2. Similarly, instant claims 1-11 and 15-20 are directed to SEQ ID NO: 14, a nucleotide sequence which encodes SEQ ID NO: 15 and SEQ ID NO: 14 merely shows the nucleotide sequence resulting from the incorporation of the nucleotide sequence of SEQ ID NO: 3 (of the '545 patent) into the nucleotide sequence of SEQ ID NO: 1 (of the '545 patent) between nucleotides 516 and 517. ***All this information is also present in the claims of the '545 patent, thus the claims of the '545 patent give a description of the instantly claimed polypeptides and polynucleotides***. The instant claims are broader in scope because they recite 50% identity (for instance, claim 1) as opposed to 70% identity in the claims of the '545

patent, however, the more specific recitation in the claims of the '545 patent anticipate the instant claims.

Conclusion

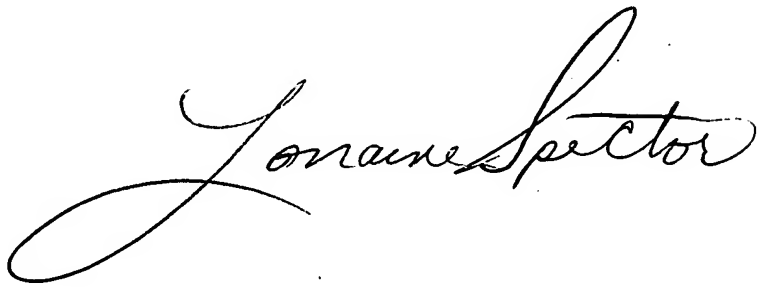
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D. can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christina Borgeest, Ph.D.



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